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(57) Abstract

The severity of metabolic disturbance in animals with cancer is mitigated by feeding the animal a nutritionally balanced food composition having a fat content of about 27 to 35 %, on a dry matter basis, a carbohydrate content of about 15 to about 27 % on a dry matter basis in which is present a mixture of arginine, omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids, the weight ratio of omega-3, omega-6 fatty acid being in the range of 0.3:1 to 3.5:1.

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THERAPEUTIC DIET FOR DOGS WITH LYMPHOMA

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to a method of reducing metabolic abnormalities found in animals with cancer and including a pet food composition effective for this purpose.

2. The Prior Art

Cancer cachexia is a complex paraneoplastic syndrome of progressive involuntary weight loss that occurs even in the face of adequate nutritional intake. For example, dogs with cancer during prolonged periods of illness, notwithstanding conventional, adequate nutritional intake, undergo a significant loss of body weight. Of major concern to those in the field of pet nutrition is the loss of body mass, i.e., muscles, organs and the like. The severe weight loss and debilitative wasting of lean body mass associated with cancer complicates the treatment of the pet and contributes to a decreased quality of life, decreased response to treatment and shortened survival time.

The precise mechanism by which the cachexia syndrome in animals with cancer operates is not completely understood. Previous studies indicate significant alterations in carbohydrate metabolism, it being observed that dogs with lymphoma and other, non-hematopoietic malignancies have elevated lactate and insulin blood levels (Vail et al, J. Vet. Int. Med. 1990; 4:8-11;Ogilvie et al, Amer. J. Vet Res., in press). The increase in lactate levels is believed to be due, at least in part, to the tumors preferentially metabolizing glucose, using anaerobic glycolysis for energy,

thereby forming lactate as an end product. The alteration in carbohydrate metabolism (hyperlactatemia, hyperinsulinemia) does not improve when dogs with lymphoma are put into remission with chemotherapy (doxorubicin) or in dogs with non-hematopoietic malignancies that have these tumors completely excised with surgery suggesting that tumors induce long-term changes in metabolism, (Ogilivie et al, Cancer 1992; 69: 233-238; Ogilvie et al, Amer. J. Vet Res., in press).

Despite the need for a pet food formulation which can be used for correction of metabolic abnormalities recognized in animals with cancer, no effective diet has been proposed or developed by the animal nutrition art. Thus the art continues to search for a diet for treating cachexia resulting from cancer.

SUMMARY OF THE INVENTION

The present invention is premised on the discovery that metabolic disturbances in animals with cancer can be treated by a diet having particular amounts of nutrients. By providing a patient with a diet high in fat (i.e., greater than 27% on a dry matter basis) and low in carbohydrate (i.e., no more than 27% on a dry matter basis) supplemented with arginine and polyunsaturated omega-3 and omega-6 fatty acids, the metabolic disturbance in an animal with cancer is ameliorated. The term dry matter basis when used herein means the nutrient content of the product after the moisture is removed.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The method of reducing metabolic disturbance in pet animals with cancer, particularly dogs, pursuant to the present invention, is provided by feeding the pet animal a food composition in which the nutrient content is comprised of 27 to about 35% on a dry matter basis of fat and about 15 to about 27% on a dry matter basis of carbohydrate supplemented to contain on a dry matter basis about 2.0 to about 3.5% arginine, about 2.5 to about 7.5% omega-3 fatty acids and about 2.0 to about 6.0% omega-6 fatty acids, the weight ratio of omega-3 to omega-6 fatty acids being in the range of about 0.3:1 to 3.5:1. The present invention is generally intended to apply to

all forms of pet food including dry, canned or intermediate moisture pet food products, as these terms are recognized by those skilled in the art of pet food formulation and manufacturing.

The pet food composition of the present invention is not intended to be restricted by any specific listing of proteinaceous, fat or carbohydrate ingredients or product form, since these will be entirely dependent upon the nutritional balance of the ration desired as well as their availability to the pet food manufacturer. Generally, aside from the nutritionally balancing ingredients such as vitamins, minerals and the like, the pet food compositions of the present invention have a moisture content of about 10 to about 90% by weight and preferably about 65 to about 75% by weight and are formulated having a nutrient content listed in Table I below.

TABLE I

Nutrient	Nutrient Content % (Dry Matter Basis)
Carbohydrate	about 15 to about 27
Protein	about 35 to about 48
Fat	about 27 to about 35
Omega-3 Fatty Acid	about 2.5 to about 7.5
Omega-6 Fatty Acid	about 2.0 to about 6.0
Arginine	about 2.0 to about 3.5
Nutritional balancing agents such as vitamins (A, B_1, B_2, B_6, E) and minerals (Ca, P, Na, K, Mg, Fe, Cl)	about 0.4 to about 1.0

A critical factor insofar as the present invention is the presence of arginine and omega-3 and omega-6 polyunsaturated fatty acids in a nutritionally balanced pet food composition containing the concentrations of fat and carbohydrate in the proportions specified in Table I above. It is the control of these latter two nutrients in the nutritionally balanced pet food composition in combination with the arginine and omega-3 and 6

polyunsaturated fatty acid nutrients that has been found to provide a remarkable reduction in the severity of metabolic abnormalities in dogs with cancer to which the food product is fed. The exact means or manner in which the fat and carbohydrate ingredients are controlled in the diet is not critical to the practice of the present invention and the respective levels of these particular ingredients in the pet food can be controlled primarily by selection of the ingredients based upon analysis or estimated fat and carbohydrate content in any of the ingredients used in the formulation of the pet food composition.

The specific dietary balance between fat and carbohydrates in combination with the specific concentrations of arginine, omega-3 and omega-6 polyunsaturated fatty acids set forth herein is believed to positively affect the negative impact of metabolic abnormalities in animals with cancer by providing a means for correcting such abnormalities in the animal.

The fat and carbohydrate nutrients used to prepare the pet food compositions of the present invention may be supplied by ingredients such as meat, meat by-products, other animal protein sources and grains as the food source. By meat is meant the flesh of cattle, swine, sheep, goat, horses, and other mammals as well as poultry and fish. Meat by-products include, but are not limited to lungs, kidneys, brain, livers, and stomachs and intestines freed of their contents. Additionally, meat, meat by-products, and other animal protein source mixtures are suitable for use in the pet food of this invention. The nutrient ingredients may also include amounts of cereal grains such as wheat, corn, barley and rice and fibrous bulking materials such as cellulose, beet pulp, peanut hulls or soy fiber.

A typical canned dog food product of the present invention is prepared from a mixture of the following ingredients:

Ingredient	% by Weight
Water	25 - 30
Lungs, Beef Lobes	40 - 45
Liver	6-10
Chicken	5-8
Rice	4-8
Fish Oil (omega-3 and omega-6 fatty acid source)	5-8
Cellulose	0.5-2
Beet Pulp	0.5-2
Inorganic Salts (calcium carbonate, iron oxide, potassium citrate)	0.5-2
Arginine	0.2-0.6
Vitamins	0.01-0.2
Taurine	0.02-0.2
Minerals	0.01-0.2

In preparing the pet food product of the present invention, the nutrient composition is adjusted so that the concentration of omega-3 polyunsaturated fatty acids is present in the animal food product of the present invention at a concentration of about 2.5 to about 7.5% on a dry matter basis and preferably about 7.0 to about 7.5% on a dry matter basis, and the omega-6 polyunsaturated fatty acid is present in the pet food product at a concentration of about 2.0 to about 6.0% on a dry matter basis and preferably about 2 to about 2.5% on a dry matter basis.

The omega-3 and omega-6 polyunsaturated fatty acids are most conveniently provided by fish oils such as menhaden, mackerel, herring, anchovy and salmon which all have significant levels of omega-3 and omega-6 polyunsaturated fatty acids. Omega-3 fatty acids C20:5 eicospentaenoic acid and C22:6 docosahexaenoic acid are typical of fish oil and together comprise about 25-38% of the fish oil. Examples

of omega-6 polyunsaturated fatty acids include linoleic acid and arachidonic acid. Sources typically are animal fats and vegetable oils such as soy, canola and corn oil.

The animal food product of the present invention is supplemented with arginine to contain about 2.0 to about 3.5% on a dry matter basis and preferably about 3.0 to about 3.5% on a dry matter basis. The arginine and fish oil components of the pet food product of the present invention are incorporated in the food product during the processing of the formulation, as for example, during and after mixing of the ingredients of the pet food. Distribution of these components can be accomplished by conventional means.

Other additives may be included in this pet food as needed. These other additives include flavoring, vitamins, minerals, coloring and mixtures thereof. These additives are added for nutritional purposes and palatability. Suitable amounts are easily determined by a person having ordinary skill in the art. However, up to about 5% of these ingredients are customarily used. Ingredients in this category are exemplified by iron oxide, sodium chloride, potassium citrate, potassium chloride, and other edible salts, flavoring, vitamins, minerals and coloring.

The pet food products of the present invention are prepared by mixing ground animal and poultry proteinaceous tissues with the remaining ingredients which include fish oils, arginine, cereal grains and other nutritionally balancing ingredients and special purpose additives such as vitamin and mineral mixtures, inorganic salts, cellulose and beet pulp bulking agents and the like. Water sufficient for processing is also added. A vessel suitable for heating while blending the components is used.

Heating of the ingredient mix may be effected in any suitable manner as, for example, by direct steam injection or by using a vessel fitted with a heat exchanger. Following the addition of the last ingredient, the mixture is heated to a temperature ranging from approximately 70∞ to about 140∞F Temperatures outside of this range are acceptable but may not be

commercially practical without the use of other processing aids. When heated to the appropriate temperature, the material is in the form of a thick liquid. The thick liquid product is then filled into cans. A lid is applied and the container is hermetically sealed. Next, the sealed can is placed into conventional equipment designed to sterilize the contents. This is usually accomplished by heating to temperatures above 230∞F for an appropriate time which is dependent on the exact temperature and formula.

For the purposes of a complete understanding of the present invention it should be recognized that the term pet food composition is generally intended to apply to commercially sold and nutritionally balanced pet food which provides the sole food intake for the pet animal.

The following Example is intended to describe specific but non-limiting embodiments of the present invention.

EXAMPLE

Preparation of Pet Food Product

A pet food product of the present invention was prepared by blending a mixture of the ingredients listed in Table II below and heating the mixture to 135°F for 15 minutes followed by filling cans at 110°F to form a thick liquid which was canned and sterilized at 250°F for 83 minutes.

Table II

Ingredient	Lbs.
Lungs, Beef	44.00
Water	26.12
Liver, Pork	8.00
Rice, Parboiled	6.00
Menhaden Oil (1)	5.75
Chicken, Mechanically Deboned	5.50
Natural Flavor *	1.50
Cellulose	1.00
Beef Pulp	1.00
Potassium Citrate	0.50
L-Arginine	0.30
Calcium Carbonate	0.10
Vitamin mix**	0.08
Mineral Mix***	0.05
Taurine	0.05
Red Iron Oxide	0.03
Choline Chloride	0.02
Total	100.00

* Available from Applied Food Biotechnologies

** Available from Roche Animal Health and Nutrition

*** Available from J. M. Huber Corp.

(1) Fatty Acid Composition of Menhaden Oil**** Fatty Acid	Wt. % of Predominant Fatty Acids (a)
Palmitic (16:0)	16.2%
Palmitoleic (16:1)	11.6%
Stearic (18:0)	2.9%
Oleic (18:1)	10.9%
Linoleic (18:2)	1.2%
Linolenic (18:3)	1.6%
Octadecatetraenoic (18:4)	3.2%
Eicosapentaenoic (20:5)	14.1%
Docosahexaenoic (22:6)	11.9%
Eicosenoic (20:1)	1.3%
Arachidonic (20:4)	1.7%
Docosapentaenoic (22:5)	2.4%

****Commercially available from Zapata Protein, Inc.

(a) Fatty acid concentrations <1% are not included

Analysis of the retorted pet food product prepared from the ingredients of Table II indicated, as recorded in Table III, the presence of the following constituents:

Table III

A. Major Nutrients

Nutrient	% by Weight	% Dry Matter
Moisture	71.6	NA
Protein	10.8	37.9
Fat	9.3	32.7
Carbohydrate	6.0	21.2
Fiber, crude	1.0	3.5
Ash	1.3	4.7
Calcium	0.15	0.5
Phosphorus	0.14	0.5
Sodium	0.08	0.3
Potassium	0.30	1.1
Magnesium	0.01	0.04
Chloride	0.12	0.42
Arginine	1.0	3.4
Omega-6 Fatty acid	0.6	2.3
Omega-3 Fatty Acid	2.1	7.3

B. Minor Nutrients

Nutrients	Units	% by weight	% Dry Matter
Copper	(mg/kg)	1.5	5.3
Iron	(mg/kg)	55	195
Manganese	(mg/kg)	5.7	20
Zinc	(mg/kg)	56	195
Selenium	(mg/kg)	0.3	1.0
Iodine	(mg/kg)	0.5	1.6
Tryptophan	%	0.6	2.2
Threonine	%	0.4	1.4
Methionine	%	0.2	0.6
Isoleucine	%	0.3	1.2
Leucine	%	0.8	2.8
Tyrosine	%	0.6	2.1
Histidine	%	0.3	0.9
Lysine	%	0.7	2.4
Taurine	%	0.6	1.9
Biotin	(mg/kg)	0.1	0.5
Choline	(mg/kg)	1070	3765
Folic Acid	(mg/kg)	0.3	1.2
Niacin	(mg/kg)	26	92
Pantothenic Acid	(mg/kg)	9	31
Riboflavin (B_2)	(mg/kg)	4	15
Pyridoxine (B_6)	(mg/kg)	3	10
Vitamin B_{12}	(mg/kg)	0.1	0.4
Thiamine (B_1)	(mg/kg)	18	64
Vitamin E	(IU/kg)	150	500
Vitamin A	(IU/kg)	25000	85000

5

A fifteen week study on the lactate and insulin blood levels of dogs with cancer fed two different pet food compositions designated "Diet 1" and "Diet 2" was initiated with twenty-eight dogs with histologically confirmed high grade stage III or IVa lymphoma, according to the World Health Organization classification scheme. Dogs were excluded from the study if they were cachectic or if they had received chemotherapy, exogenous steroids, or anesthesia in the 30 days before their selection for the study. In addition, dogs with concurrent diseases such as renal failure, hepatic cirrhosis, endocrine diseases, obesity, or hypercalcemia secondary to lymphoma were excluded. Eighteen dogs were stage IIIa (generalized lymph node involvement, without systemic signs) and ten dogs were stage IVa (clinical evidence of liver and/or spleen involvement, without systemic signs). Median and mean weights of the dogs were 22kg and 24kg, respectively with a range from 5kg to 30kg. Ages of the dogs ranged from 3.5 to 13 years with a median of 7 years and a mean of 7 years.

All dogs were randomized blindly into one of two groups and exclusively fed water and either Diet 1 or Diet 2. Diet 1 was the nutritionally balanced, high fat/low carbohydrate dog food supplemented with arginine and omega-3 and omega-6 fatty acids prepared in accordance with the Example. Diet 2 was a control which had the same composition as Diet 1 except the arginine and omega-3 and omega-6 fatty acid supplements were not included in the food formulation.

To determine the effect of Diets 1 and 2 on the metabolic dysfunction of the dogs, intravenous glucose tolerance tests and diet tolerance tests were conducted. Each study was performed prior to initiation of diet therapy and cancer chemotherapy. This period is identified as the pretreatment period in Tables IV-VII. Three, 6, 9, 12 and 15 weeks following initiation of diet and cancer chemotherapy, the intravenous glucose tolerance tests and diet tolerance tests were repeated.

- Intravenous Glucose Tolerance Test (IVGTT) and Concomitant Lactate and Insulin Levels

Following an overnight 12 hour fast, blood was taken before and 5, 15, 30, 45, and 60 minutes following the intravenous administration of 500 mg/kg of 25% dextrose over 30 seconds. Samples were stored at -20°C immediately after collection and assayed together at a later time. Lactate concentrations were determined on serum by a semi-automated enzymatic method (YSI Glucose, 2700 Select Lactate Analyzer, Yellow Springs, Ohio). Serum insulin concentrations were determined in duplicate by radioimmunoassay techniques with a commercially available kit (Catalog #07-160102, ICN Biomedicals Inc., Carcon, CA.).

- Diet Tolerance Test (DTT) and Concomitant Lactate and Insulin Levels

Following an overnight 12 hour fast, blood was taken before, immediately after, and 5, 15, 30, 45, 60, 90, 120, 180, 240, 300, and 360 minutes after dogs were allowed to consume either Diet 1 or Diet 2, that they were randomized to receive. The amount fed was calculated as 1/2 [70 (body weight$_{kg}$ $^{0.75}$)]. Samples were taken for analysis of lactate and insulin. Samples were stored at -20°C immediately after collection and assayed together at a later time. Lactate and insulin were determined as described above.

The results of the IVGTT and DTT tests are summarized in Tables IV-VII below. In these Tables the terms "Diet 1" and "Diet 2" mean the dogs fed Diet 1 and Diet 2 in the 15 week study.

The results recorded in Tables IV through VII show the effectiveness of the incorporation of arginine and omega-3 and omega-6 polyunsaturated fatty acids in a high fat/low carbohydrate pet food fed to dogs with cancer to mitigate metabolic disturbance.

For example, in the IVGTT, lactate and insulin concentrations normalize in the Diet 1 group. More specifically, the lactate and insulin concentrations significantly decrease in the dogs fed Diet 1, but not in the Diet 2 (control) group compared to pre-treatment values. The development of elevated lactate and insulin concentrations in response to a glucose challenge is substantially reduced in the Diet 1 group when compared to the Diet 2 group.

In the Diet Tolerance Test, the data are exactly as described above for intravenous glucose tolerance testing. Dogs fed Diet 1 normalized lactate and insulin levels and produced less lactate and insulin in response to the diet challenge as compared to dogs fed Diet 2.

Table IV
Glucose ToleranceTest
Lactate in Plasma (mg/dl)

		Minutes					
Test Period		0	5	15	30	45	60
Pre-Treatment*	Diet 1a	15	15	18	17	15	14
	Diet 2	13	14	17	19	17	15
Post-Treatment**							
3 weeks	Diet 1b	9	9	10	11	10	9
	Diet 2	10	11	13	16	15	13
15 weeks	Diet 1b	9	8	10	10	9	7
	Diet 2	11	12	13	17	15	12

* Prior to initiation of diet and cancer treatment.
** Weeks following initiation of diet and cancer treatment.
a,b Dogs fed Diet 1 had significantly different serum lactate values at all time points at 3 and 15 weeks post-treatment.

Table V
Glucose ToleranceTest
Insulin in Plasma (uU/dl)

		Minutes					
Test Period		0	5	15	30	45	60
Pre-Treatment*	Diet 1	24a	98a	112a	58	36a	27a
	Diet 2	28	71	86	55	34	28
Post-Treatment**							
3 weeks	Diet 1	21	83b	93	53	22b	18b
	Diet 2	26	82	100	64	44	24
15 weeks	Diet 1	14	87	87b	56	21b	14b
	Diet 2	26	82	100	64	44	24

* Prior to initiation of diet and cancer treatment.
** Weeks following initiation of diet and cancer treatment.
a,b Dogs fed Diet 1 had significantly different serum insulin values at 5, 45 and 60 minutes at 3 weeks post-treatment and 0, 15, 45,and 60 minutes at 15 weeks post-treatment compared to pretreatment.

Table VI
Diet ToleranceTest
Lactate in Plasma (mg/dl)

		Minutes after Feeding											
Test Period	Group	0	5	15	30	45	60	90	120	180	240	300	360
Pre-Treatment	Diet 1a	12.9	12.9	13.3	13.4	13.8	13.5	14.0	13.8	12.2	10.6	9.1	9.1
	Diet 2	13.4c	13.4	15.1c	14.1c	14.1c	14.9	16.1	14.0	12.1	11.1	9.9	9.7c
Post-Treatment**													
3 weeks	Diet 1	7.6	7.0	7.2	8.3	8.6	8.8	8.8	7.5	6.3	4.9	4.7	4.1
	Diet 2	11.7	10.9	11.8	12.9	14.8	15.4	15.2	15.3	10.2	7.7	6.8	6.1
6 weeks	Diet 1b	8.9	7.1	8.0	8.6	10.3	10.1	8.8	8.3	6.1	5.1	4.4	4.3
	Diet 2	9.7	10.3	10.3	11.5	14.2	15.5	14.4	13.0	10.7	8.5	7.1	6.3
9 weeks	Diet 1b	6.4	6.1	9.0	7.7	7.9	8.3	8.6	7.7	5.5	4.5	4.5	5.2
	Diet 2	11.1	10.9	10.7	12.2	14.5	14.8	14.2	14.6	10.8	8.6	7.2	6.5
12 weeks	Diet 1b	6.3	5.7	6.0	6.8	7.4	7.9	8.7	8.0	5.8	5.3	4.6	4.4
	Diet 2	10.6d	10.2	9.7d	10.4d	11.6d	13.8	16.0	12.3	10.3	8.4	8.1	6.5d

* Prior to initiation of diet and cancer treatment.

** Weeks following initiation of diet and cancer treatment.

a,b Dogs fed Diet 1 had significantly different serum lactate values across all time points at 6, 9, & 12 weeks post-treatment compared to pre-treatment.

c,d Dogs fed Diet 2 had significantly different serum lactate values at 0, 15, 30, 45, and 360 minutes at 12 weeks compared to pretreatment.

Table VII
Diet ToleranceTest
Insulin in Plasma (μU/dl)

		Minutes after Feeding											
Test Period	Group	0	5	15	30	45	60	90	120	180	240	300	360
Pre-Treatment*	Diet 1	58	36a	37	38	41	35	34	42	38	39a	34	37
	Diet 2	65	41	38	31	32c	41	26	32	25c	29	30	29
Post-Treatment**													
3 weeks	Diet 1	32	24b	23	25	27	28	26	27	23	26b	25	27
	Diet 2	54	40	35	35	40	37	38	27	33	44	32	23
6 weeks	Diet 1	20	26b	31	26	25	25	24	23	28	27b	28	28
	Diet 2	53	23	26	26	35	31	34	33	32	27	29	29
9 weeks	Diet 1	25	23b	26	28	28	32	29	28	27	27b	28	28
	Diet 2	72	31	26	33	44d	34	26	41	42d	25	33	30
12 weeks	Diet 1	29	29b	28	26	27	25	26	27	27	30b	29	29
	Diet 2	56	34	43	42	34	46	45	38	47	43	31	31

* Prior to initiation of diet and cancer treatment.
** Weeks following initiation of diet and cancer treatment.
a,b Dogs fed Diet 1 had significantly different serum insulin values at 5 and 240 minutes at 3, 6, 9, & 12 weeks compared to pretreatment.
c,d Dogs fed Diet 2 had significantly different serum insulin values at 45 and 180 minutes at 9 weeks compared to pretreatment.

CLAIMS

What is claimed is

1. A method for mitigating the severity of metabolic disturbances in animals with cancer comprising (a) forming a nutritionally balanced petfood composition having a fat content of about 27 to 35% on a dry matter basis, a carbohydrate content of about 15 to about 27% on a dry matter basis in which is also present a mixture of arginine, omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids, and (b) feeding the composition to the animal with cancer.

2. The method of claim 1 wherein arginine is present in the food composition at a concentration of about 2.0 to about 3.5% on a dry matter basis.

3. The method of claim 1 wherein the omega-3 polyunsaturated fatty acid is present in the food composition at a concentration of about 2.5 to about 7.5% on a dry matter basis.

4. The method of claim 1 wherein the omega-6 polyunsaturated acid is present in the food composition at a concentration of about 2.0 about 6.0% on a dry matter basis.

5. The method of claim 1 wherein the weight ratio of omega-3 polyunsaturated fatty acid to omega-6 fatty acids is about 0.3:1 - 3.5:1

6. A food composition for mitigating the severity of metabolic disturbance in animals with cancer comprising (a) a nutritionally balanced food having a fat content of about 27 to 35% on a dry matter basis, a carbohydrate content of about 15 to about 27% on a dry matter basis in which is present a mixture of arginine, omega-3 polyunsaturated fatty acids and omega-6 polyunsaturated fatty acids, the weight ratio of omega- 3 to omega-6 fatty acid being in the range of about 0.3:1 to 3.5:1.

7. The composition of claim 6 wherein arginine is present in the food composition at a concentration of about 2.0 to about 3.5% on a dry matter basis.

8. The composition of claim 6 wherein the omega-3 polyunsaturated fatty acid is present in the food composition at a concentration of about 2.5 to about 7.5% by on a dry matter basis.

9. The composition of claim 6 wherein the omega-6 polyunsaturated acid is present in the food composition at a concentration of about 2.0 to about 6.0% by on a dry matter basis.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 96/15865

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A23K1/16 A23K1/18 A61K31/195 A61K31/20 A61K31/23

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A23K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CANCER, vol. 71, no. 10, 1993, PHILADELPHIA, US, pages 3146-3152, XP000617658 G.K. OGILVIE ET AL.: "Energy expenditure in dogs with lymphoma fed two specialized diets" see page 3146, column 1, paragraph 1 - column 2, paragraph 3 ---	1,6
A	EP 0 567 433 A (SANDOZ NUTRITION LTD) 27 October 1993 see page 6, line 10 - line 20 see claims 1,3,11,14-18 --- -/--	1,6

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
11 February 1997	20.02.97

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Dekeirel, M

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 96/15865

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE WPI Section Ch, Week 9411 Derwent Publications Ltd., London, GB; Class B05, AN 94-088611 XP002024955 & JP 06 038 708 A (EARTH SEIYAKU KK) , 15 February 1994 see abstract	1,6
A	EP 0 026 985 A (GEN FOODS CORP) 15 April 1981 see claims 1,5,6,10	1,6
A	FASEB JOURNAL FOR EXPERIMENTAL BIOLOGY, vol. 9, no. 4, 1995, BETHESDA, MD US, page A863 XP002024954 S.L. MILLER ET AL.: "Low-dose parenteral arginine does not affect glucose utilization in vivo" see page A863, column 1, abstract 5003	1
A	PATENT ABSTRACTS OF JAPAN vol. 013, no. 529 (C-658), 27 November 1989 & JP 01 215245 A (SUNTORY LTD), 29 August 1989, see abstract	1,6
A	EP 0 609 056 A (KYOWA HAKKO KOGYO KK) 3 August 1994 see page 3, line 9 - line 10 see claims 1,2,6	1,3,4,6, 8,9
A	BREAST CANCER RESEARCH AND TREATMENT, vol. 13, no. 1, 1989, BOSTON, US, pages 49-60, XP000617654 F.S. SHOFER ET AL.: "Histopathologic and dietary prognostic factors for canine mammary carcinoma" see page 49, Summary	1,6
A	AMERICAN JOURNAL OF EPIDEMIOLOGY, vol. 133, no. 7, 1991, BALTIMORE, US, pages 694-703, XP000617669 E.G. SONNENSCHEIN ET AL.: "Body conformation, diet, and risk of breast cancer in pet dogs: a case-control study" see page 694, Summary	1,6

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INTERNATIONAL SEARCH REPORT

Inte onal Application No
PCT/US 96/15865

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,A	EP 0 678 247 A (IAMS COMPANY) 25 October 1995 see page 2, line 16 - line 34 see page 3, line 37 - line 57 see page 6, line 18 - line 32 see examples 1-4 see claims 1-20 -----	1,3-6,8, 9

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Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

national application No.
PCT/US 96/ 15865

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Claims searched completely: 6-9 Claims searched incompletely: 1-5
REMARK: Although claims 1-5 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searches without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

information on patent family members

Inte ional Application No
PCT/US 96/15865

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP-A-0567433	27-10-93	AT-T-	143570	15-10-96
		AU-A-	3706493	28-10-93
		CA-A-	2094540	24-10-93
		DE-D-	69305105	07-11-96
		ES-T-	2092266	16-11-96
		JP-A-	6009384	18-01-94
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EP-A-0678247	25-10-95	AU-A-	1652095	26-10-95
		CA-A-	2147109	19-10-95
		JP-A-	8038063	13-02-96